Claims

1. Peptidic compounds having covalently closed bridge structures, which branch off from suitable amino acid side chains of a peptidic binding molecule with alpha-helical conformation and which connect at least two amino acid side chains of this peptide which are located at positions i and i+ 7 of the amino acid sequence of the peptide, thereby stabilizing the bridged part of the helix and being characterized by the presence of at least one amide (peptide) bond and at least one disulfide bridge, which both form part of the bridge backbone.

2. Peptidic compounds according to claim 1, wherein the bridge backbone ,including the side chain atoms of amino acids I and I + 7 of the peptidic binding molecule, consists of one or two amide (peptide) bonds, one disulfide bridge and further 7 to 11, preferably 9 C- or N-atoms.

3. Peptidic compounds according to claim 2, wherein the bridge backbone comprises two amide (peptide) bonds, one sulfide bridge and further 7 carbon atoms.

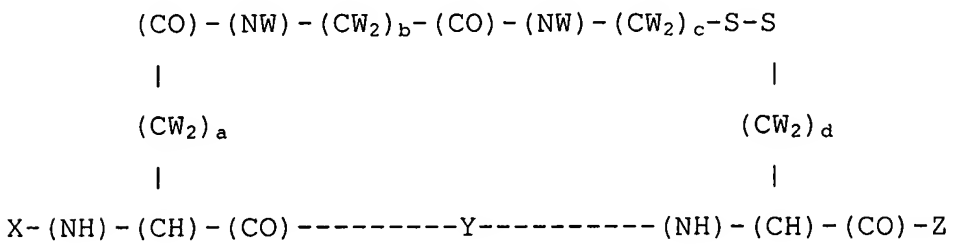
4. Peptidic compounds according to claims 1 to 3, wherein the bridge is stabilized by one or more amino acid side chain(s) of the peptidic binding molecule by hydrogen bonds and the stabilizing amino acid(s) have a position between the two braching points of the bridge.

5. Peptidic compounds according to claim 4, wherein the stabilizing amino acid(s) are selected from lysine, arginine, arparagine, glutamine, aspartic acid, glutamic acid, serine, threonine, thyrosine, or histidine.

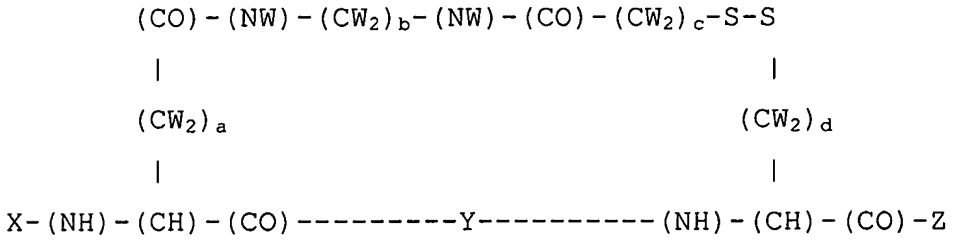
6. Peptidic compounds according to claim 5, wherein the stabilizing amino acid(s) is/are located at position(s) i + 3 and/or i + 4 of the peptides.

7. Peptidic compounds according to claim 6, wherein the stabilizing amino acid(s) is/are aspartate at position i + 3, and/or lysine or glutamine at position i + 4

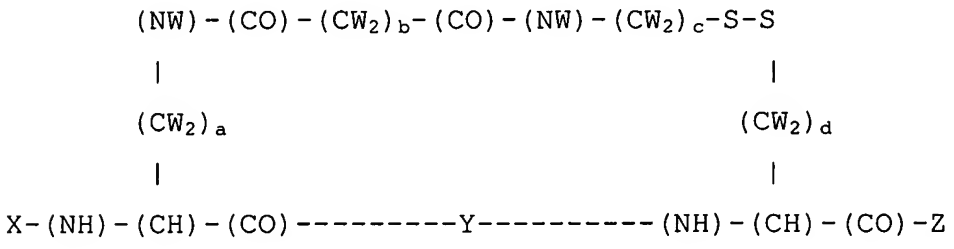
8. Peptides compounds according to claims 1-7, and represented by the molecules covered by) one of the formulas (1a) – (1d):



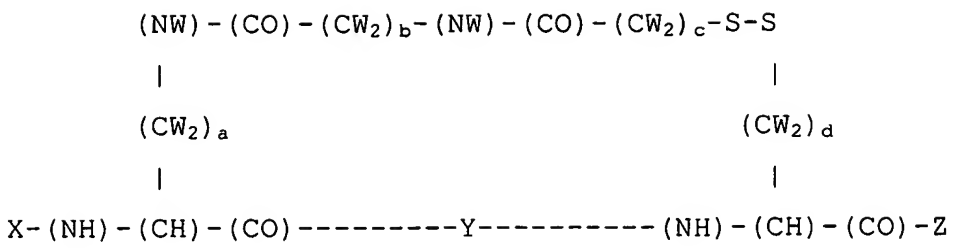
(1a)



(1b)



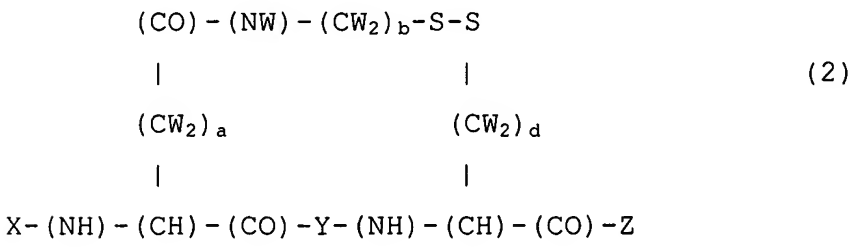
(1c)



(1d)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1), (2) or (3); a, b, c and d are independently selected from the integers 1 to 3, provided that the sum a+b+c+d is 7, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

9. Peptidic compounds according to claim 1-7, and represented by the molecules covered by the generic formula (2):

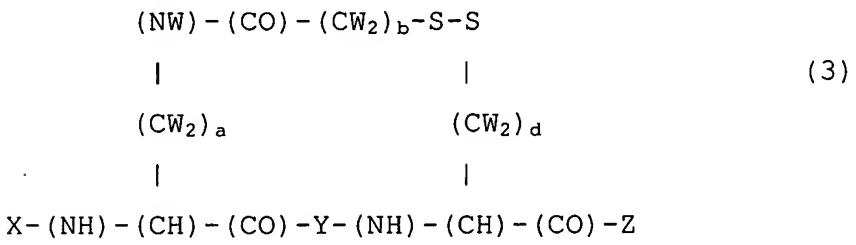


(2)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), a, b and d are

independently selected from the integers 1 to 5, provided that a+b+d is 9; at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

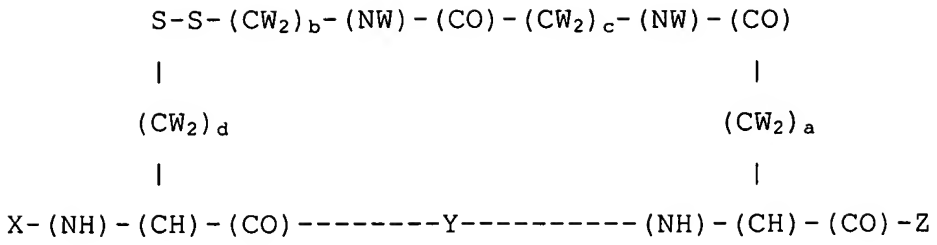
10. Peptidic compounds according to claim 1-7, and represented by the molecules covered by the generic formula (3):



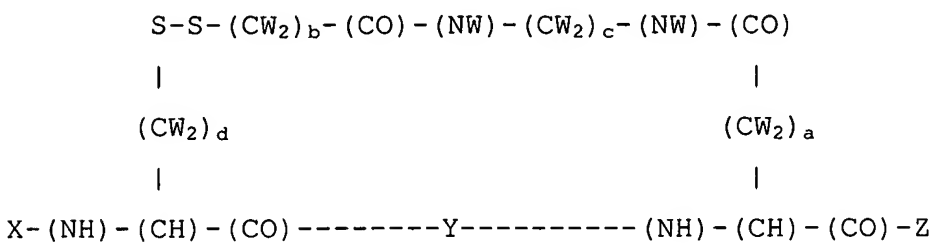
(3)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1), (2) or (3), a, b and d are independently selected from the integers 1 to 5, provided that a+b+d is 9, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

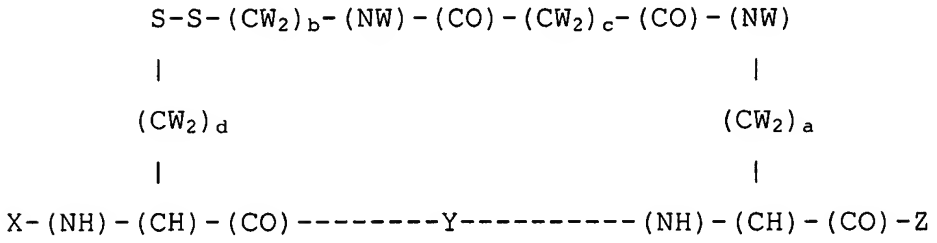
11. Peptidic compounds according to claim 1-7, and represented by the molecules covered by one of the formulas (4a) – (4d):



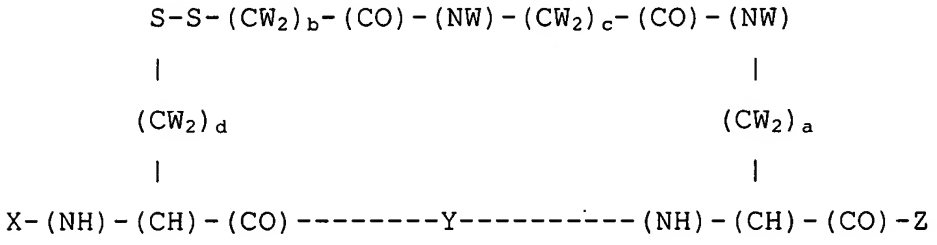
(4a)



(4b)



(4c)

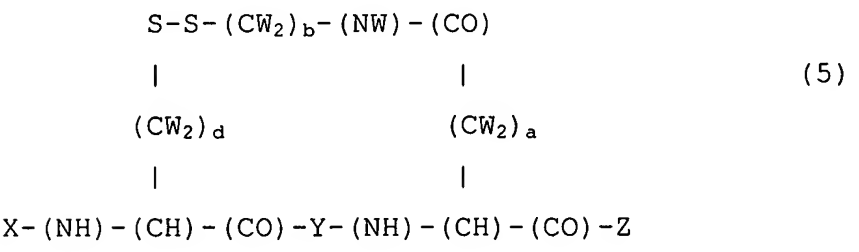


(4d)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1) to (2), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1) to (6), a, b, c and d are independently selected from the integers 1 to 3, provided that a+b+c+d is 7, at each

independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

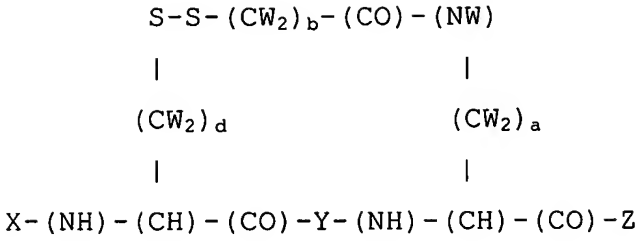
12. Peptidic compounds according to claim 1-7, and represented by the molecules covered by the generic formula (5):



(5)

wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1) to (6), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1) to (6), a, b and d are independently selected from the integers 1 to 5, provided that a+b+d is 9, W is hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a peptide of maximally 30 amino acids, a polyethyleneglycol moiety, or a naturally occurring or artifical sugar molecule and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

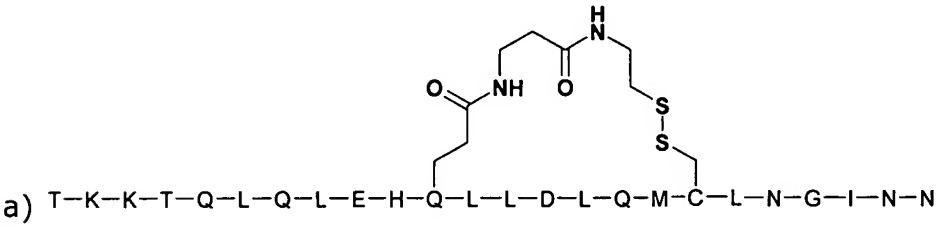
13. Peptidic compounds according to claim 1-7, and represented by the molecules covered by the generic formula (6):

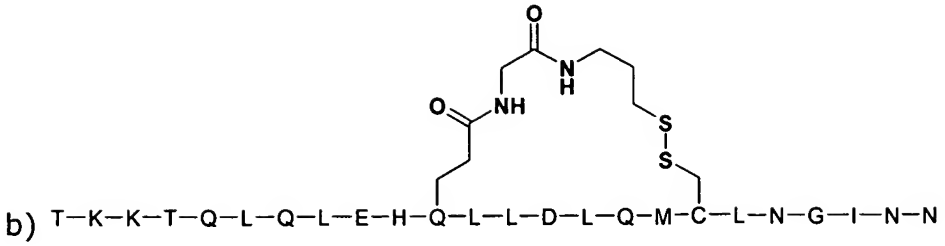


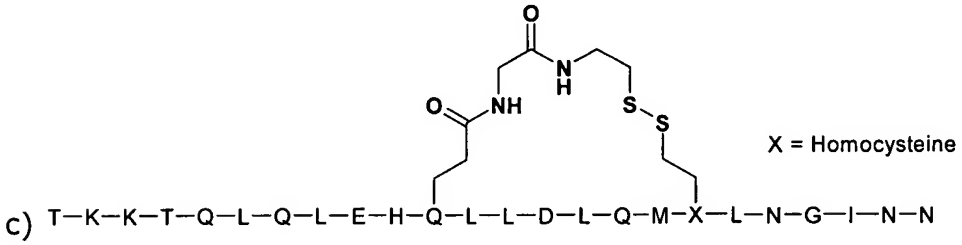
(6)

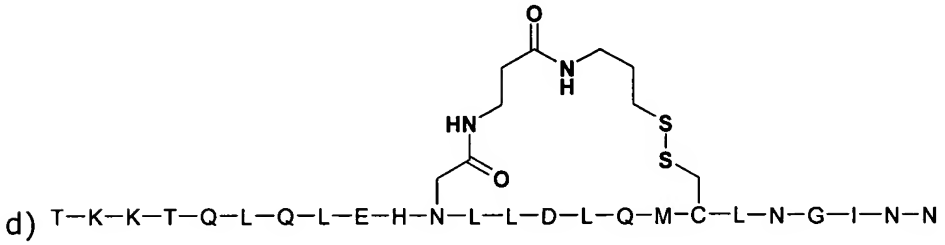
wherein X is hydrogen or any amino acid or any peptide or any compound represented by formula (1) to (6), Y is any amino acid sequence consisting of six amino acids, Z is hydroxyl or any amino acid or any peptide or any compound represented by formula (1) to (6), a, b and d are independently selected from the integers 1 to 5, provided that a+b+d is 9, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule, and the peptides can consist of natural and/or unnatural D- and/or L-amino acids.

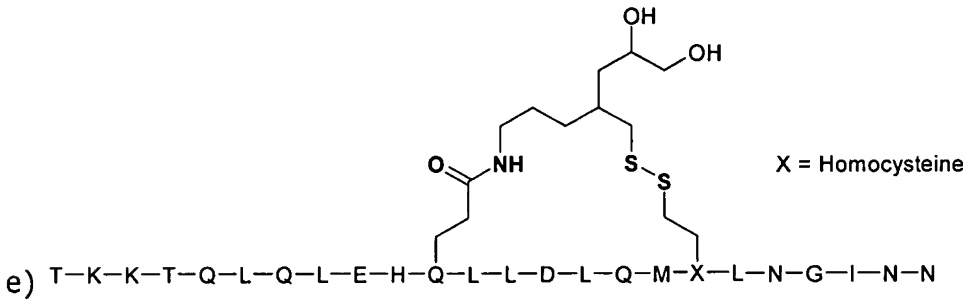
14. Peptidic compounds according to claims 1-13, binding to the interleukin 2 receptor and containing the stabilized peptide sequence TKKTQLQLEHKLLDLQMXLNGINN in a helical conformation, where X stands for homocysteine and two helical turns are bridged by a backbone according to claims 1-13; thereby including non-exclusively the sequences and structures (a- f) as follows:

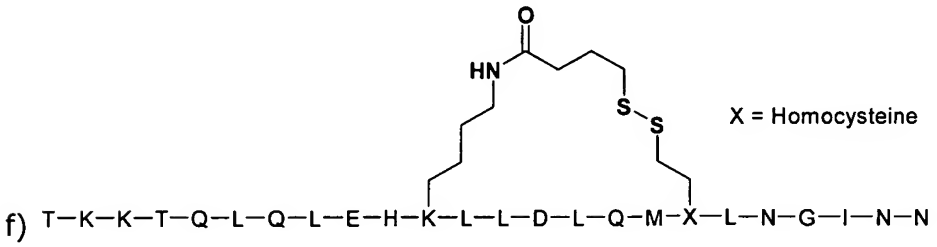
a) 











15. Peptidic compounds according to Claim 14, in which the bridging structure is shifted along the peptide sequence in such a way that binding to the

interleukin 2 receptor is maintained and another part of the overall helical structure is bridged by the construct.

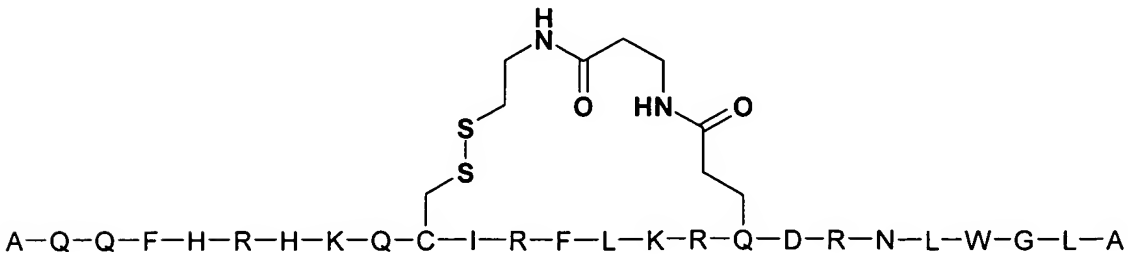
16. Peptidic compounds according to claims 14 and 15, in which at least one amino acid of the peptide sequence is replaced by physicochemically related natural or non-natural amino acids in a conservative exchange, which maintains the binding of the peptide to the Interleukin 2 Receptor.

17. Peptidic compounds according to claims 14-16, which are N- and/or C-terminally modified in such a way that the binding of the peptide to the Interleukin 2 receptor is maintained and/or water solubility is improved and/or that exopeptidases can not cleave at the terminal sites, whereby terminal modifications include non-natural amino acids, D-amino acids, sugar moieties or freely chosen appropriate organic moieties.

18. Pharmaceutical preparations containing an active ingredient according to claims 14-17 and intended for use in humans or animals as an antagonist of the action of the cytokine Interleukin 2.

19. Peptidic compounds according to claims 1-13, binding to the interleukin 4 receptor and containing the stabilised peptide sequence AQQFHRHQCIRFLKRQDRNLWGLA in a helical conformation, wherein two helical turns are bridged by a backbone according to claims 1-13; thereby including non-exclusively the following sequence and structure (g):

g)



20. Peptidic compounds according to claim 19, in which the bridging structure is shifted along the peptide sequence in such a way that binding to the interleukin 4 receptor is maintained and another part of the overall helical structure is bridged by the construct.

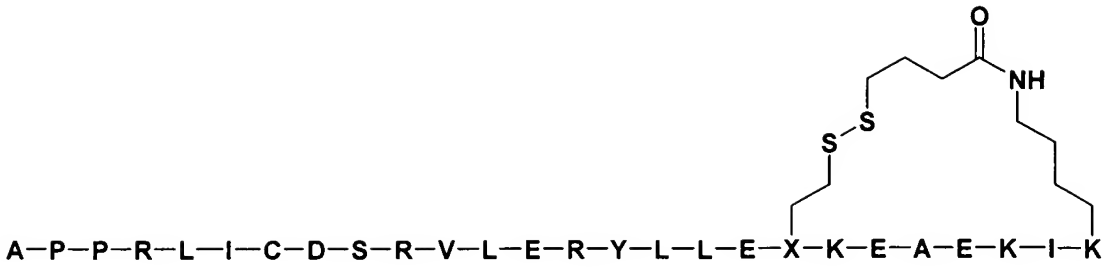
21. Peptidic compounds according to claims 19-20, in which at least one amino acid of the peptide sequence is replaced by physicochemically related natural or non-natural amino acids in a conservative exchange, which maintains the binding of the peptide to the Interleukin 4 receptor.

22. Peptidic compounds according to claims 19-21, which are N- and/or C-terminally modified in such a way that the binding of the peptide to the Interleukin 4 receptor is maintained and/or water solubility is improved and/or that exopeptidases can not cleave at the terminal sites, whereby terminal modifications include non-natural amino acids, D-amino acids, sugar moieties or freely chosen appropriate organic moieties.

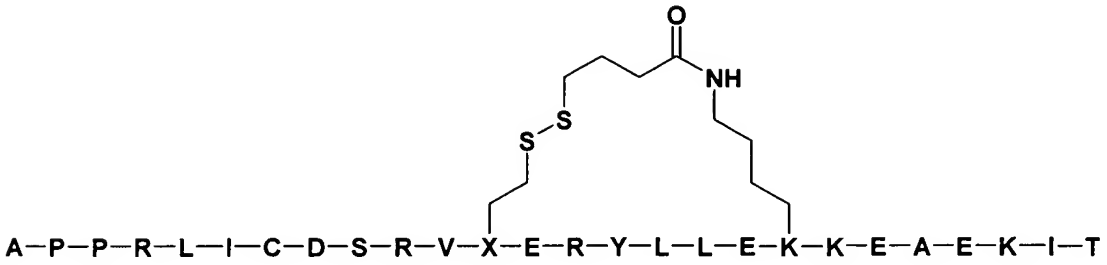
23. Pharmaceutical preparations containing an active ingredient according to claims 19-21 and intended for use in humans or animals as an antagonist of the action of the cytokine Interleukin 4.

24. Peptidic compounds according to claims 1- 13, binding to the erythropoietin receptor and containing the stabilised peptide sequence APPRLICDSRVLERYLLEXKEAEKIK in a helical conformation, wherein two helical turns are bridged by a backbone according to claims 1-13; thereby including non-exclusively the following sequences and structures (h-i):

h)



i)



25. Peptidic compounds according to Claim 24, in which the bridging structure is shifted along the peptide sequence in such a way that binding to the erythropoietin receptor is maintained and another part of the overall helical structure is bridged by the construct.

26. Peptidic compounds according to claims 24-25, in which at least one amino acid of the peptide sequence is replaced by physicochemically related natural or non-natural amino acids in a conservative exchange, which maintains the binding of the peptide to the erythropoietin receptor.

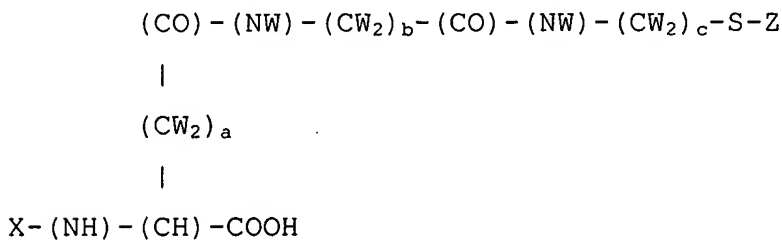
27. Peptidic compounds according to claims 24-26, which are N- and/or C-terminally modified in such a way that the binding of the peptide to the erythropoietin receptor is maintained and/or water solubility is improved and/or that exopeptidases can not cleave at the terminal sites, whereby terminal modifications include non-natural amino acids, D-amino acids, sugar moieties or freely chosen appropriate organic moieties.

28. Pharmaceutical preparations containing an active ingredient according to claims 19-22 and intended for use in humans or animals as an agonist of the action of the cytokine erythropoietin.

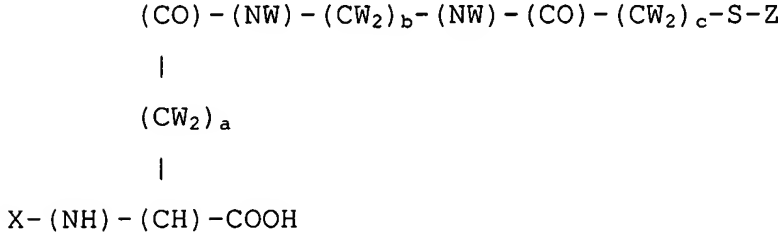
29. Mono- and polyclonal antibodies to the substances covered by Claims 1-28, and the use of such antibodies in diagnostic and pharmacological quantification and/ or inhibition of action of the active substances in body fluids or tissues of animals or humans.

30. Peptidic compounds according to claims 1-17, 19-22 and/or 24-27, in which the N-terminal amino acid is acetylated and/or the C-terminal amino acid is amidated.

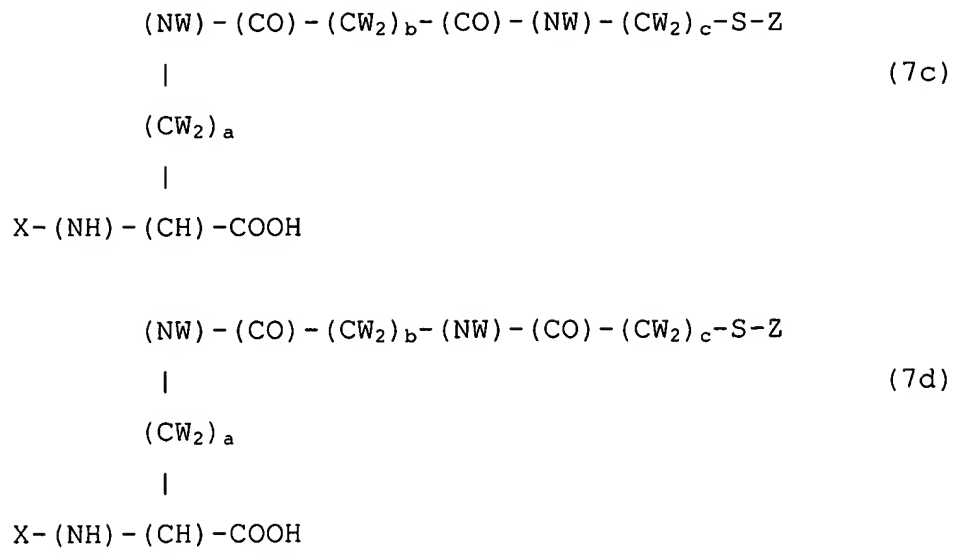
31. Compounds as building blocks for the synthesis of peptidic compounds of any of claims 1-17, 19-22 and/or 24-27, represented by the molecules covered by the generic formulas (7a) to (7d):



(7a)



(7b)

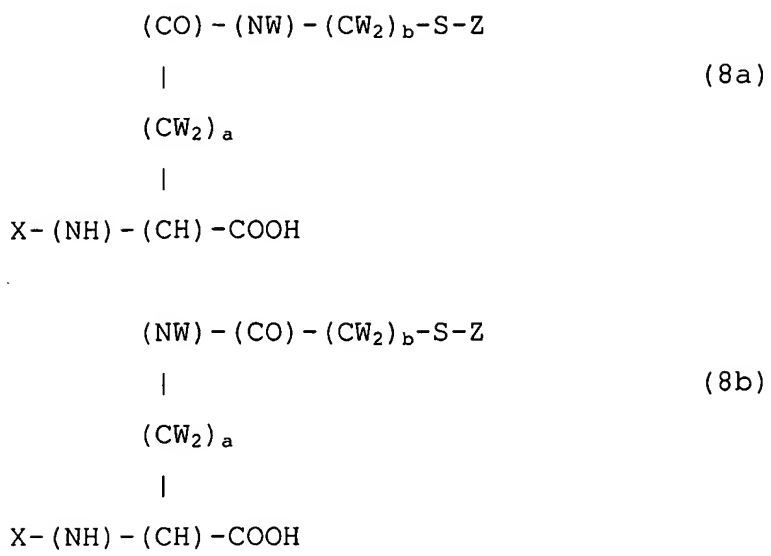


(7c)

(7d)

wherein X and Z are hydrogen or any protecting group; a, b, and c are independently selected from the integers 1 to 3, provided that the sum a+b+c is an integer from 3 to 6, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule.

32. Compounds as building blocks for synthesis of peptidic compounds of any of claims 1-17, 19-22 and/or 24-27, represented by one of the formulas (8a) to (8b):

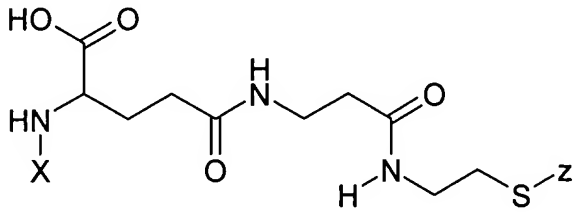


(8a)

(8b)

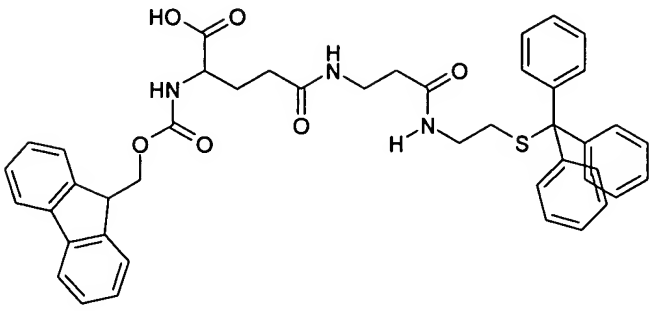
wherein X and Z are hydrogen or any protecting group; a and b are independently selected from the integers 1 to 5, provided that the sum a+b is an integer from 2 to 8, at each independent position of W, W can be freely chosen from hydrogen, a hydroxyl-, carboxyl- or amino group, an alkyl moiety with at least one hydroxyl-, carboxyl- or amino group, a polyethyleneglycol moiety, or a naturally occurring or artificial sugar molecule.

33. Compounds of claim 31 of the formula (9), wherein X and Z are hydrogen or any protecting group:



(9)

34. A compound of claim 33 of the formula (10):



(10)

35. Methods for synthesis of building blocks according to claims 31 to 34 via solid phase synthesis.

36. Methods for synthesis of peptidic compounds according to claims 1-17, 19-22 and/or 24-27 comprising the following steps:

a. Synthesizing an intermediate peptidic compound by means of peptide synthesis from C- to N-term, comprising introduction of an amino acid containing a protected SH function in its sidechain at position *i+7* (i.e. introduction after deprotection of the N-term of the amino acid at position *i+8*), followed by the introduction of six amino acids at positions *i+6* to *i+1*, and furthermore followed by introduction of a building block according claims 31-34 at position *i* (i.e. after deprotection of the N-term of the amino acid at position *i+1*) of the growing peptide chain,
b. continuation of the peptide synthesis until the N-terminal amino acid was introduced
c. Removal of the remaining protecting groups,
d. establishing helix-stabilizing conditions, for example with appropriate fluorinated solvents,
e. obtaining the peptidic compound by closure of a disulfide bridge with appropriate reagents under these helix-stabilizing conditions.